REMARKS

Applicants have cancelled the previously withdrawn claims 1-17 and 28-40.

Applicant has amended claims 18, 19, 25 and 26, and added new claims 41-50. Claims have been amended to expedite prosecution and, at minimum, to reduce issues on appeal.

Claims 18, 19, 25 and 26 have been amended to limit them to detection of thymidine substitution at position 825 of SEQ ID NO:2. New claims 41-50 are directed to detecting a substitution at position 1429 of SEQ ID NO:2. The amendment and the new claims are supported by the specification as a whole and by the original claims. Thus, the amendment introduces no new matter and its entry is respectfully requested.

Applicant has amended claims 18, 19, 25 and 26 to correct the typographical error in the term "thymine" by replacing it with a typographically correct term "thymine." The amendment is of typographical nature and thus does not introduce new matter and its entry is respectfully requested.

Claim 18 has been further amended to refer to detection of the genetic modification in a nucleic acid encoding SEQ ID NO:2 by adding the phrase "by detecting the genetic modification in the nucleic acid comprising SEQ ID NO: 2." The amendment is supported specifically, for example, at page 9, lines 6-12. Thus the amendment does not introduce new matter and its entry is respectfully requested.

Claims 18 and 19 have been amended further by adding a description as to how one correlates the genetic modification to the responsiveness of the individual to the in vivo pharmaceutical by adding a phrase "and wherein the thymidine at position 825 of SEQ ID NO: 2 is indicative of the individual having increased activation capacity of G proteins which is indicative of the reduced responsiveness of the individual to the...." The amendment is supported specifically, for example, at page 12, lines 8-9 and at page 34, lines 12-25. Thus the amendment does not introduce new matter and its entry is respectfully requested.

Claim 19 has also been amended to correct a typographical error by deleting the duplicate "to" from the line 2 of the claim. As a typographical error this amendment introduces no new matter and its entry is respectfully requested.

Claims 25 and 26 have been amended to include a functional description as to how evaluation of the individual is performed. Amendment to claim 25 is specifically supported, for example, page 35, lines 12-25. Amendment to claim 26 is specifically supported, for example, page 36, lines 10-11. Therefore, no new matter is introduced by these amendments and their entry is respectfully requested.

With regard to Applicant's claim for foreign priority, Applicant herewith submit that the certified copies and certified translations of the non-English priority documents. Entry of the documents is respectfully requested.

As indicated on the Application Data Sheet submitted on March 12, 2001, and on the first paragraph of the specification, this application is a continuation in part of PCT/EP99/06534, filed September 6, 1999. Applicant herewith submit the priority documents. Accordingly, applicant respectfully request that the application be awarded September 6, 1999 priority date.

Turning now to the specific rejections.

Claims 18 – 19 stand rejected under U.S.C. §102(a) as being anticipated by Zill et al. and by Naber et al.

Zill et al. was published in June 2000 and Naber et al. was published in November 2000. Therefore, neither of these references is prior art in light of the September 6, 1999 priority date of this application. Accordingly, Applicant respectfully request that these rejections be withdrawn to reduce the issues on appeal.

Claims 18 – 27 stand rejected under 35 U.S.C. §112, second paragraph.

Although applicant respectfully disagrees, applicant has amended claims to expedite prosecution, or, at minimum, to reduce the issues on appeal. Applicant requests that this rejection be withdrawn for the following reasons.

Examiner contends that the recited "evaluation of genetic modification" is not clear. Although applicant submits that the phrase is clear to one skilled in the art, applicant has amended claim 18 to recite specifically to evaluating a nucleic acid comprising the SEQ ID NO:2 for the substitution.

Moreover, the examiner contends that the claims are vague because there is no step that explains how the evaluation of the mutation results in evaluation of the individual's response to an in vivo pharmaceutical. Although applicant submits that the specification clearly teaches how this evaluation is performed and the term is therefore clear, applicant has amended claims 18 and 19 to recite to the presence of the T-allele being indicative of the individual having a reduced response to the pharmaceuticals. Applicant has further amended claim 25 and 26 to include the correlation of genotype to a specific phenotype. Accordingly, claim 25 now recites 825T allele being associated with increased reduction of cardiac output when the individual is administered beta-adrenoreceptor blockers, and claim 26 recites 825T allele being associated with reduced response to substances having E1 prostaglandin action.

Applicants submit that the claims now clearly describe how the "evaluating responsiveness of an individual" is performed. Therefore, in light of these amendments, applicant submits that the rejection under 35 U.S.C. §112, second paragraph should be withdrawn.

Claims 18 – 27 stand rejected under 35 U.S.C. §112, first paragraph.

The Examiner takes the position that the specification does not provide enablement for methods for evaluating responsiveness of an individual to any *in vivo* pharmaceutical by assaying for a thymine at position 825 or a thymine at position 1429 of SEQ ID NO: 1.

Applicant respectfully disagree and request that this rejection be withdrawn for the following reasons.

To expedite prosecution, or at minimum, to reduce the issues on appeal, applicant has divided the claims in to two groups: claims 18-27 are directed to subject matter relating to the

polymorphism at position 825, and claims 41-50 are directed to subject matter relating to polymorphism at position 1429.

Applicant submits that the test for enablement is whether one reasonably skilled in the art could make or use the invention, without undue experimentation, from the disclosure in the patent specification coupled with information known in the art at the time the patent application was filed. U.S. v. Telectronics Inc., 857 F.2d 778, 8 USPQ 2d 1217 (Fed. Cir. 1988).

Enablement is not precluded even if some experimentation such as routine screening is necessary. Hybritech, Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1384 (Fed. Cir. 1986), cert denied, 480 U.S. 947. This is even so if the amount of experimentation required is laborious. In re Wands, 858 F.2d 731 (Fed. Cir. 1988). An invention meets the standard for successfully practice set by Section 112 unless the invention is "totally incapable of achieving a useful result." Brooktree v. Advances Micro Devices, 24 USPQ 2d 1401, 1412 (Fed. Cir. 1992).

Further, it is well established that compliance with the enablement requirement of 35 U.S.C. §112, first paragraph, does not require the disclosure of a working example at all. An embodiment of the claimed invention can be based on predicted results rather than work actually conducted or results actually achieved. See Gould v. Quigg, 822 F.2d 1974, 1078; 3 USPQ 2d 1302, 1304 (Fed. Cir. 1987). The specification need not contain an example if the invention is otherwise disclosed in such a manner that one skilled in the art will be able to practice it without an undue amount of experimentation. In re Borkowski, 422 F.2d 904, 908; 164 USPQ 642, 645 (CCPA 1970).

Claims 18 – 27, directed to a method for evaluating responsiveness of an individual to an *in vivo* pharmaceutical are fully enabled throughout the specification. In section one, starting at page 11 through section 14 at page 35, the application discusses the detail of the application of the present invention in prediction of diabetes mellitus (type II), adiposity/obesity, coronary heart disease and atherosclerosis, increased cholesterol, increased immune system function, increased t-lymphocyte, intensified progression of AIDS, osteoporosis, Alzheimer's Disease, erectile dysfunction, thyroid gland dysfunctions, increased pregnancy risks and low birth rate.

Applicant submits that the teaching provided in these sections of the application and the

knowledge and level of a reasonably skilled artisan would enable one to practice the claimed invention without undue experimentation.

In view of the above remarks, Applicant requests that this rejection, under 35 U.S.C. 112, first paragraph, be withdrawn.

In view of the foregoing amendment it is respectfully submitted that all claims are in condition for allowance. Early and favorable action is requested.

If any additional fee is required, charge Deposit Account No. 50-0850.

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Respectfully submitted,

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